

Docket No.: 215177.00101
Customer No. 27160

HICKMAN
Application No. 09/575,377

Amendments to the Claims:

Claims 1 – 50 (Cancelled)

51. (New) A method for identifying one or more ion channels of a cell that may be affected by a test substance by deconvoluting a change in cell membrane potential, comprising: exposing a test substance to a device and accompanying software,

in which said device comprises:

(a) a solid state microelectrode array;

(b) a cell culture comprising one or more electrically active cells having a cell membrane including one or more ion channels, which cells are capable of providing a measurable action potential that exhibits one or more perceptible characteristics in response to a test substance;

(c) an intervening layer which (i) comprises a surface modifying agent, and (ii) is positioned between said microelectrode and said one or more cells of said cell culture, that provides a high impedance seal with said one or more cells and allows a deconvolution step to be performed, and

(d) accompanying deconvolution software with instructions that can be implemented by a computer and which relate changes in the characteristics exhibited by the action potential to one or more ion channels of said one or more cells upon exposure to the test substance.

52. (New) The method of claim 51, wherein the one or more characteristics exhibited by said action potential is manifested in its waveform or a derivative thereof.

53. (New) The method of claim 52, in which the one or more characteristics include at least one of after potential, time to cessation of activity, frequency, amplitude, shape, spike rate, or time constant.

54. (New) The method of claim 51, in which the instructions comprise data processing instructions capable of receiving input data comprising data on ion flux through ion channels selected from the group consisting of sodium channels, potassium channels, calcium channels, and combinations thereof.

55. (New) The method of claim 51, in which the microelectrode is planar or flexible.

Docket No.: 215177.00101
Customer No. 27160

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56. (New) The method of claim 51, in which the microelectrode is a field effect transducer.

57. (New) The method of claim 51, which further comprises an insulator layer outside the microelectrode selected from the group consisting of silicon, modified silicon dioxide, silicon nitride, silicon carbide, germanium, silica, gallium, arsenide, epoxy resin, polystyrene, polysulfone, alumina, silicone, fluoropolymer, polyester, acrylic copolymers, polylactate, or combinations thereof.

58. (New) The method of claim 51 in which said electrically active cell comprises a neuronal cell or a cardiac cell.

59. (New) The method of claim 58 in which the neuronal cell is a hippocampal cell.

60. (New) The method of claim 51 in which the cell culture comprises a stem cell, a transformed stem cell, their respective progeny, or a combination thereof.

61. (New) The method of claim 10 in which the stem cell is exposed to a differentiating factor.

62. (New) The method of claim 51 in which the surface modifying agent comprises a self-assembling monolayer or monolayers.

63. (New) The method of claim 62 in which the self-assembling monolayer comprises a silane, a thiol, isocyanide, polyelectrolyte or combinations thereof.

64. (New) The method of claim 51, wherein the intervening layer further comprises cell anchorage molecules selected from the group consisting of antibodies, antigens, receptor ligands, receptors, lectins, carbohydrates, enzymes, enzyme inhibitors, biotin, avidin, streptavidin, RGD-type peptides, integrins, cadherins, modified lipids, and combinations thereof.

65. (New) The method of claim 51, wherein the intervening layer further comprises a high viscosity mixture comprising alcohols, ethers, esters, ketones, amides, glycols, amino acids, saccharides, carboxymethylsaccharides, carboxyethylsaccharides, aminosaccharides, acylaminosaccharides, polymers thereof, or combinations thereof.

66. (New) The method of claim 51 in which one or more cells are transfected with endogenous or exogenous nucleic acid.

Docket No.: 215177.00101
Customer No. 27160

HICKMAN
Application No. 09/575,377

67. (New) The method of claim 66 in which the nucleic acid comprises a nucleotide sequence associated with known or unknown function.

68. (New) The method of claim 51, wherein the cell culture is coated with a polymer.

69. (New) The method of claim 68 in which the polymer comprises cellulose, methylcellulose, or dextran.

70. (New) The method of claim 1, wherein a second layer is in contact with the electrically active cells and is attractive to cell adherence.

71. (New) The method of claim 51 in which the test substance comprises a toxin, a drug, a pathogen, a neurotransmitter, a nerve agent, or mixtures thereof.

72. (New) The method of claim 51 in which the deconvolution of cell membrane potential includes deconvoluting the cell action potential or its derivative.

73. (New) The method of claim 72 in which deconvolution of the action potential or its derivatives provides information on pathways in the cell affected by the test substance.